

REMARKS

1. Preliminary Remarks

a. Status of Claims

Claims 69-72, 89-96 are pending and under active consideration. Claims 69-72 are allowed. Claims 89 and 96 are amended. Claims 90, 91, 94, and 95 are canceled. Applicant respectfully requests entry of the amendments and remarks made herein into the file history of this application. Upon entry of the amendments, claims 69-72, 89, 92, 93, and 96 will be pending and under active consideration.

b. Amendment to the Claims

In order to expedite prosecution and without prejudice to seeking claims of similar scope in a continuing application, Applicant has canceled claims 90, 91, 94, and 95 without prejudice. Claim 89 has been amended in part (c), which is now directed to an isolated nucleic consisting of X nucleotides wherein the sequence of the nucleic acid comprises a sequence at least 80% identical to Y consecutive nucleotides of SEQ ID NO: 2 or 9, or an RNA encoded by Y consecutive nucleotides of SEQ ID NO: 2 or 9, wherein $X = 19$ to 140 , $Y \geq 19$, and $X \geq Y$. Support for amended claim 89 can be found throughout the specification, for example, paragraph 0049.

Claim 96 have been amended and is now directed to a vector comprising a heterologous sequence, wherein the heterologous sequence consists of the sequence of the nucleic acid of claims 69-72, 89, 92, 93, and 96. Support for amended claim 96 can be found throughout the specification, for example, paragraph 0039. One of ordinary skill in the art would recognize that features other than the heterologous sequence would be necessary for a functional vector.

2. Patentability Remarks

On pages 2-4 of the Office Action, the Examiner rejects claims 89-91 and 96 under 35 U.S.C. §112, first paragraph, for failing to comply with the written description requirement. Specifically, the Examiner asserts that the limitations “a sequence 68.2% identical to (a) or (b),” “a sequence at least 81.9% identical to (a) or (b),” and “a sequence at least 91.0% identical to (a) or (b)” lack support in the disclosure. Applicant respectfully traverses.

As acknowledged by the Examiner on page 4 of the Office Action, the specification describes that miRNAs can bind to target genes with less than 100% complementary, but asserts that the specification does not appear to provide a description sufficient to support a genus of molecules now encompassed by the claims. Applicant disagrees with regard to sufficient description. As discussed in our response filed June 11, 2007, the specification provides numerous examples of the claimed miRNAs as set forth in SEQ ID NOS: 2 and 9 binding target genes with less than 100% complementarity. For example, Table 7, lines 188035-188829 of the specification shows examples of the claimed miRNAs sequences as set forth in

SEQ ID NOS: 2 and 9 binding various target gene sequences with 68.2%, 81.9%, and 91.0% complementarity (See Appendix A).

The Examiner however states on page 3 of the Office Action that a text search of “68.2%”, “81.9%”, and “91.0%” was unsuccessful. Applicant submits that the alignments shown in Table 7 provide the inherent written descriptive support of these percent variants by calculating the percentage of the number of bases that align between the miRNA sequence and the target gene sequence. One of skill in the art can reasonably conclude that the inventor had possession of the claimed invention by the alignments described in Table 7.

Nevertheless, in order to expedite prosecution, claim 89 has been amended as described above because the specification does clearly provide textual support at paragraph 0049 for at least 80% variants of the claimed miRNA sequences as set forth in SEQ ID NOS: 2 and 9 that bind and repress expression of mRNA transcripts of particular target genes. As discussed above, claims 90 and 91 have been canceled without prejudice and claim 96 draws its dependency in part from claim 89. In view of the foregoing amendment and remarks, Applicant respectfully request that the rejection of claims 89-91 and 96 under 35 U.S.C. §112, first paragraph for allegedly lacking proper written description support has been overcome and should be withdrawn.

3. Conclusion

Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification of to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

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APPENDIX A

Table 7, lines 188035-188829 disclose that the miRNA GAM3298 (SEQ ID NO: 2) is capable of binding to sites within 326 target gene mRNAs. Table 7 further discloses that 15 out of 22 nucleotides (68.2%) of GAM3298 are sufficient for binding target mRNAs. For example, 68.2% of the residues of SEQ ID NO: 2 are capable of targeting mRNAs of the genes HIP1 and ADCY1, as follows:

GAM NAME SEQUENCE	GAM RNA	TARGET REF-ID	TARGET	UTR	TARGET	BS-SEQ (UPPER: GAM; LOWER: TARGET)	BINDING-SITE DRAW	GAM POS
GAM3298	AAAGTGGTCAT AGTGCAGGTAG	HIP1	NM_005338.3	3	ACGCCTGTAATCC CAGCACTTT	AAAGTGCT TTTCACGA	CATAG TGCAGGT ATGTCGG CCCTA CA	A
GAM3298	AAAGTGGTCAT AGTGCAGGTAG	ADCY1	NM_021116.1	3	TGTTTGCACTATA CTTT	AAAGT TTTCA	GCTC ATAGTGCA TATCAGGT TT	A

Table 7 also discloses that the mRNA GAM2608 (SEQ ID NO: 9) is capable of binding to sites within 117 target gene mRNAs. Table 7 further discloses that 15 out of 22 nucleotides (68.2%) of GAM2608 are sufficient for binding target gene mRNAs. For example, 68.2% of the residues of SEQ ID NO: 9 are capable of targeting mRNAs of the genes CALCB and EGR4, as follows:

GAM2608	TAAGGTGCATC TAGTGCACTTA	CALCB	NM_000728.2	3	TAATTGCCCTGTC ACCTTT	T AAGGTGCA TTCCACGT T	TCTAGT GCAGTTA CGTTAAT CCC---	A
GAM2608	TAAGGTGCATC TAGTGCACTTA	EGR4	NM_001965.1	3	TAAGTGCACACGC CCCACGCCTTC	T AAGGTG TTCCGC C	CATCTA-- GTGCACTTA CACGTCAAT ACCCCGCA	A

Table 7 discloses that 18 out of 22 nucleotides (81.9%) of the miRNA GAM3298 (SEQ ID NO: 2) are sufficient for binding target gene mRNAs. For example, 81.9% of the residues of SEQ ID NO: 2 are capable of targeting mRNAs of the genes ABCC3 and ADSL, as follows:

GAM3298	AAAGTGGTCAT AGTGCAGGTAG	ABCC3	NM_020037.1	3	TACCTGCACGTGTC CTGACCATCGCAC	AAA GTGC CAGC ---	----- TCA AGT CTACC CCT	A
GAM3298	AAAGTGGTCAT AGTGCAGGTAG	ADSL	NM_000026.1	3	TTACCTTAAATTA GTACAGCACTTT	CA-- AAAGTGCT TTTCACGA	GC-- TAGT ATTA CATG AAT	A

Table 7 also discloses that 18 out of 22 nucleotides (81.9%) of the miRNA GAM2608 (SEQ ID NO: 9) are sufficient for binding target gene mRNAs. For example, 81.9% of the residues of SEQ ID NO: 9 are capable of targeting mRNAs of the genes ABCC3 and CASP3, as follows:

GAM2608	TAAGGTGCATC TAGTGCAGTTA	ABCC3	NM_020038.1	3	TAGCAAACTCTGG GGGCACCTTA	AT TAAGGTGC ATTCCACG GG	CA-- CTAGTG GGTCAC AAA	GTTA CGAT	A
GAM2608	TAAGGTGCATC TAGTGCAGTTA	CASP3	NM_032991.1	3	TAATGCAATTTTA GACCATTAT	TA AGGTG TTTAC TA	CA TCTA AGAT C-	-- GTGTCAGTTA TACGTCAAT TT	A

Table 7 discloses that 20 out of 22 nucleotides (91.0%) of the miRNA GAM3298 (SEQ ID NO: 2) are sufficient for binding target gene mRNAs. For example, 91.0% of the residues of SEQ ID NO: 2 are capable of targeting mRNAs of the genes ASTN and MECP2, as follows:

GAM3298	AAAGTGCTCAT AGTGCAGGTAG	ASTN	XM_045113.2	3	ATGCCAGGCGCTG ATGTAAGCACTTT	-- AAAGTGCT TTTCACGA AT	- CAT GTA G	A- AGTGC TCGCG GA	G GGTA CCGT A	A
GAM3298	AAAGTGCTCAT AGTGCAGGTAG	MECP2	NM_004992.2	3	TTATTTGCACTAT TGAGTCTTC	A AAG TTC C	T GCTCA TGAGT -	- TAGTGCAGGTAG ATCAGTTTATT T		A

Table 7 also discloses that 20 out of 22 nucleotides (91.0%) of the miRNA GAM2608 (SEQ ID NO: 9) are sufficient for binding target gene mRNAs. For example, 91.0% of the residues of SEQ ID NO: 9 are capable of targeting mRNAs of the genes MAP4K5 and MMP26, as follows:

GAM2608	TAAGGTGCATC TAGTGCAGTTA	MAP4K5	NM_006575.2	3	AAACTGCACATG ATTGCTTTA	C TAAGGTG ATTTCGT T	- ATC TAG T	A TAGTGCAGTT ATCAGTCAA A		A
GAM2608	TAAGGTGCATC TAGTGCAGTTA	MMP26	NM_021801.2	3	AACTGAAAGCACT AGAGCAGCCTTG	- TAAGG GTTCC G	A TGC ACG -	---- TCTAGTGC AGATCAGC AAAG	AGTT TCAA	A